

### **REMARKS**

Claims 1, 4-5, 11, 13, 14 and 15 have been amended. No new matter has been added. Support for the amendments may be found throughout the specification and in the claims. Claim 3 has been cancelled.

Applicants thank the Examiner for acknowledgment of Applicants' claim for priority and for consideration of the Information Disclosure Statement.

Claims 1-2 and 4-15 are pending.

### **SPECIFICATION**

The Examiner has objected to the specification due to informalities. See Office Action at p. 2. Applicants have amended the specification to correct the typographical errors on page 1, line 16, page 6, line 22, page 7, line 16, page 9, line 19 and page 29, line 4.

### **CLAIM OBJECTIONS**

The Examiner has objected to claim 4 for an informality. See Office Action at p. 2. Applicants have amended claim 4 and the phrase "NH<sub>2</sub> free groups" has been removed. Applicants respectfully request the withdrawal of this objection.

The Examiner has objected to claim 11 for a misspelling. Applicants have corrected the typographical error in claim 11. Applicants respectfully request the withdrawal of this objection.

### **DRAWINGS**

Applicants thank the Examiner for the recommendation that the heading "Brief Description of Drawings" precede the description of drawings. The specification has been amended to insert the section heading as suggested by the Examiner.

### **CLAIM REJECTIONS**

#### ***Rejection of claims under 35 U.S.C. § 112, first paragraph***

The Examiner has rejected claim 1 under 35 U.S.C. § 112, first paragraph, because "the specification, while being enabling for a specific 'compound presenting free NH<sub>2</sub> groups' (e.g.

$C_{10}$ - $C_{24}$  alkylamine) and a specific ‘antibody’ (e.g. AMB8LK), does not reasonably provide enablement for all compounds with free  $NH_2$  groups and all antibodies.” See Office Action at p. 3. In an effort to expedite prosecution and not in acquiescence to the rejection, Applicants have amended claim 1 to refer to a cationic lipid selected from the group consisting of a  $C_{10}$ - $C_{24}$  alkylamine, a  $C_{10}$ - $C_{24}$  alkanolamine and a cholesterol ester, instead of compound presenting free  $NH_2$  groups.

With respect to the Examiner’s objection against “antibody”, Applicants respectfully submit that the invention is directed to an emulsion comprising one cationic lipid selected from the group consisting of a  $C_{10}$ - $C_{24}$  alkylamine, a  $C_{10}$ - $C_{24}$  alkanolamine and a cholesterol ester, said lipid being linked to an antibody by a heterobifunctional linker. The product of the invention aims to be a vehicle to target a drug via an antibody against antigens expressed on specific cells. As the heterobifunctional linker used in the invention interacts with the hinge regions, which do no vary depending on the antibody, the present invention can be carried out with any antibody without any undue experimentation.

Therefore, the specification enables a person skilled in the art to use the invention commensurate in scope with the claim and undue experimentation would not be required for one person skilled in the art to link the hinge region of any antibody to a heterobifunctional linker. Applicants respectfully request the withdrawal of this rejection.

***Rejection of claims under 35 U.S.C. § 112, second paragraph***

The Examiner has rejected claims 14-15 under 35 U.S.C. § 112, second paragraph, “as being indefinite ....” See Office Action at p. 5. Specifically, the Examiner considers the phrase “with the other products necessary” to be indefinite. Id.

Applicants have amended claims 14-15 to clarify the phrase “with the other products necessary to obtain an emulsion” to include water, oil and an emulsifying agent. Applicants respectfully request the withdrawal of this rejection.

***Rejection of claims under 35 U.S.C. § 102***

The Examiner has rejected claims 1-2 and 7-11 under 35 U.S.C. § 102(b) as being anticipated by WO 01/52889 to Kadouche et al. ("Kadouche"). See Office Action at p. 6. Claims 2 and 7-11 depend from independent claim 1.

Kadouche discloses an anti-ferritin antibody which can be coupled to liposome-type vector or cationic emulsion. Kadouche does not describe a combination product that includes a positive oil in water emulsion wherein the emulsion includes at least one cationic lipid selected from the group consisting of a C<sub>10</sub>-C<sub>24</sub> alkylamine, a C<sub>10</sub>-C<sub>24</sub> alkanolamine and a cholesterol ester, at the oil-water interface, and an antibody, wherein the compound is linked to the antibody by a heterobifunctional linker.

Since claims 2-14 depend on claim 1, they are patentable over the Kadouche for at least the reasons described above. Applicants respectfully request reconsideration and withdrawal of this rejection.

***Rejection of claims under 35 U.S.C. § 103***

The Examiner has rejected claims 3-6 and 12-15 under 35 U.S.C. § 103(a) as being unpatentable over Kadouche in view of Yang et al, Drug Development Research, 2000 ("Yang") and further in view of Kirpotin et al., Biochemistry, 1997 ("Kirpotin"). See Office Action at p. 7. Claims 4-6 and 12-15 depend from independent claim 1. Claim 3 has been cancelled thus rendering this rejection moot with respect to claim 3.

Kadouche relates to the use, in the manufacturing of a therapeutic drug for treating cancer linked to an overexpression of the product of a gene from the myc family, of an anti-ferritin antibody. See Abstract. Kadouche discloses that the anti-ferritin antibody can be coupled to liposome-type vector or cationic emulsion ([0064]. As previously discussed, Kadouche does not teach or suggest a combination product that includes a positive oil in water emulsion wherein the emulsion includes at least one cationic lipid selected from the group consisting of a C<sub>10</sub>-C<sub>24</sub> alkylamine, a C<sub>10</sub>-C<sub>24</sub> alkanolamine and a cholesterol ester, at the oil-water interface, and an antibody, wherein the compound is linked to the antibody by a heterobifunctional linker.

This defect is not remedied in Yang. Yang relates to the state of the art of positively charged submicron emulsions. See Abstract of Yang. Yang describes emulsions that include natural or semisynthetic lipids, fatty acids and oils and optionally cationic surfactant (stearylamine, oleylamine), non ionic surfactant (poloxamers) and phospholipids. See page 477, right column, first paragraph of Yang. Yang does not teach or suggest a combination product that includes a positive oil in water emulsion wherein the emulsion includes at least one cationic lipid selected from the group consisting of a C<sub>10</sub>-C<sub>24</sub> alkylamine, a C<sub>10</sub>-C<sub>24</sub> alkanolamine and a cholesterol ester, at the oil-water interface, and an antibody, wherein the compound is linked to the antibody by a heterobifunctional linker.

The Examiner contends that “[a] person having ordinary skill in the art at the time the invention was made would have found it obvious to combine the teaching of Kadouche (antibody coupled to a cationic emulsion) with the cationic lipids taught by Yang.” See Office Action at p. 8. However, such a person would not have been able to succeed in his experiment as he would not have known how to couple the antibody to the emulsion.

This defect is also not remedied in Kirpotin. Kirpotin describes liposomes conjugated to Fab' fragments of a humanized recombinant Mab. See Abstract. Kirpotin does not teach or suggest a combination product that includes a positive oil in water emulsion wherein the emulsion includes at least one cationic lipid selected from the group consisting of a C<sub>10</sub>-C<sub>24</sub> alkylamine, a C<sub>10</sub>-C<sub>24</sub> alkanolamine and a cholesterol ester, at the oil-water interface, and an antibody, wherein the compound is linked to the antibody by a heterobifunctional linker.

None of the above-cited references, alone or in combination, teach or suggest a combination product that includes a positive oil in water emulsion wherein the emulsion includes at least one cationic lipid selected from the group consisting of a C<sub>10</sub>-C<sub>24</sub> alkylamine, a C<sub>10</sub>-C<sub>24</sub> alkanolamine and a cholesterol ester, at the oil-water interface, and an antibody, wherein the compound is linked to the antibody by a heterobifunctional linker.

Since claims 4-6 and 12-15 depend from claim 1, they are patentable over the combination of Kadouche, Yang and Kirpotin for at least the reasons described above. Applicants respectfully request reconsideration and withdrawal of this rejection.

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**CONCLUSION**

Applicants believe that the claims are in condition for allowance.

A petition for a one-month extension of time is attached.

Should any fees be required by the present Reply, the Commissioner is hereby authorized to charge Deposit Account 19-4293.

Respectfully submitted,



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